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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,827	04/14/2006	Ernst Kusters	33395-US-PCT	6756

1095 7590 11/17/2008

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
KLINKEL, KORTNEY L	
ART UNIT	PAPER NUMBER
1611	
MAIL DATE	DELIVERY MODE
11/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,827	KUSTERS ET AL.	
	Examiner	Art Unit	
	Kortney L. Klinkel	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,9 and 10* is/are pending in the application.

4a) Of the above claim(s) *3-5,9 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2 and 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/14/2006 and 4/9/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

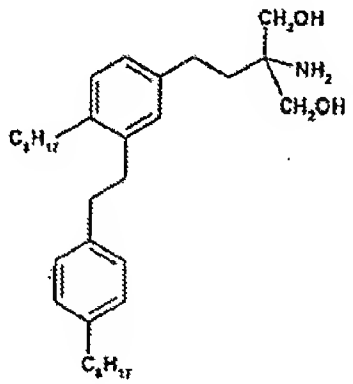
Claims

Claims 1-6 and 9-10 are pending in the instant Office action.

Election/Restriction

Applicant's election without traverse of Group I, claims 1-2, 4-6 and 9 in the reply filed on October 15, 2008 is acknowledged.

Acknowledgement is also made of Applicant's election of the compound, 2-amino-2-(2-{4-octyl-3-[2-(4-octylphenyl)-ethyl]-phenyl}-ethyl)-propane-1,3-diol that is described in Example 1 at page 4 of the specification which has the following structure:



Acknowledgement is also made of Applicant's further election of the absence of a second drug substance. Claims 1, 2 and 6 are generic to the elected species.

Claims 3-5, and 9-10 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on October 15, 2008.

As stated in the Election/Restriction requirement dated 9/15/2008, at pages 7-8, should the product claims or generic claim be found allowable, the withdrawn claims will be considered for rejoinder.

Information Disclosure Statement

Acknowledgement is made of applicant's submitting information disclosure statements on 4/14/2006 and 4/9/2008. The submissions are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

Foreign Priority

Acknowledgement is made of applicant's foreign priority claim to United Kingdom patent application serial number 0324210.4 filed 10/15/2003. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

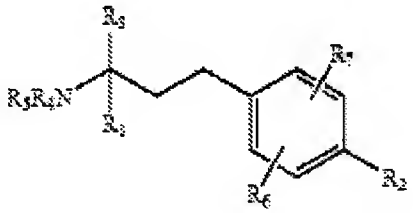
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2 and 6 are rejected under 35 U.S.C. 103(a) as being obvious over Ehrhardt et al. (US 2007/0010494).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject

matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Ehrhardt teaches compounds of the following generic structure (paragraph [0015]) which are useful as immunosuppressants, specifically as S1P receptor agonists ([0066]):



Wherein R1 is C1-6alkyl substituted by hydroxyl, *inter alia*, R3 is CH_2OH, *inter alia*, R4 and R5 are independently H, C1-4alkyl or acyl, R2 is C1-10alkyl or C1-10haloalkyl. Optionally R2, as just described can be substituted by phenyl which may optionally be substituted by C1-4alkyl ([0005]). Additionally Ehrhardt teaches a compound, FTY720 (col. 4 line 64 to col. 5 line 8), which has the same amino-1,3-diol head group as the elected species as well as the C8-alkyl chain off the first aryl group.

Ehrhardt also teaches a pharmaceutical composition comprising said compounds in association with a pharmaceutically acceptable diluent or carrier (claim 8).

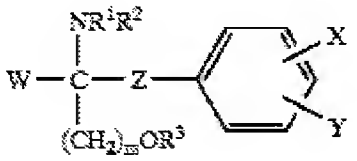
Ehrhardt fails to teach a specific example of the elected species (the compound of example 1 at page 4) as well as a C8-alkyl substitution off the second phenyl ring, but rather teaches the presence of a C1-4alkyl.

However, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to arrive at the elected species, based on the teachings of Ehrhardt with a reasonable expectation for success. One would have been motivated to do so because Ehrhardt teaches a generic structure consisting of a finite number of compounds that fully encompasses the elected species with the exception of the alkyl substituent off the second phenyl ring which are useful as S1P receptor agonists, the same utility as the instant compound. Although Ehrhardt teaches a C1-4alkyl substituent and the instant compound requires a C8-alkyl substituent, it would have been obvious to manipulate Ehrhardt's compounds for the following reasons. The compounds taught by Ehrhardt are structurally very similar to the elected species. Structurally similar compounds are expected to have similar behavior. The compounds of Ehrhardt are useful as S1P receptor agonists, which is allegedly the same as the instant compound. Furthermore, the substitution of one alkyl chain for another is well within the purview of the ordinarily skilled artisan. Such substitutions are done routinely in order to obtain a compound of optimal properties, such as melting point, hydrophobicity, solubility etc. The coupling reaction to synthesize the C1-4alkyl substituted compound and the C8-alkyl compound is the same, namely the coupling of a 4-alkyl-1-vinyl-benzene with the aryl bromide of the headgroup in the presence of a palladium catalyst.

Applicant's data in the specification has been considered. The specification states at page 6 that the compounds of formula I exhibit valuable pharmacological properties such as agonism of S1P receptors as indicated by in vitro and in vivo tests. The specification then outlines various in vitro and in vivo tests and then state that compound of formula I deplete peripheral blood lymphocytes when administered at a dose of 0.03 to 3 mg/kg. There are no specific results for individual compounds. There is no indication from the specification that the compound of the elected species exhibits results that are unexpected based on the teachings of Ehrhardt.

Claims 1-2 and 6 are rejected under 35 U.S.C. 103(a) as being obvious over Chiba et al. (US 6004565).

Chiba teaches compounds of the following generic structure (col. 3, line 44-col 4. line 40) which are useful as immunosuppressants:



Wherein W is C1-6 alkyl substituted by 1 to 3 hydroxy groups, inter alia, m is 1-3, R1, R2 and R3 are hydrogen, alkyl or acyl, X is a straight-chain alkyl having p number of carbons, or the straight chain alkyl may have 1-3 substituents including phenyl which may have 1-3 substituents including alkyl inter alia, Y is alkyl, inter alia and Z is a straight-chin alkylene having q number of carbon atoms. p and q are the same or different and each is an integer of 1 to 20 with the proviso that p + q is between and

including 6 and 23. Additionally Chiba teaches a compound, FTY720 (abstract), which has the same amino-1,3-diol head group as the elected species as well as the C8-alkyl chain off the first aryl group.

Chiba also teaches a pharmaceutical composition comprising said compounds in association with a pharmaceutically acceptable diluent or carrier (column 8, lines 19-28).

Chiba fails to teach a specific example of the elected species (the compound of example 1 at page 4) but rather teaches a structure which generically encompasses the elected compound.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to arrive at the elected species, based on the teachings of Chiba with a reasonable expectation for success. One would have been motivated to do so because Chiba teaches a generic structure consisting of a finite number of compounds that fully encompasses the elected species which are useful as immunosuppressants, the same utility as the instant compound.

Applicant's data in the specification has been considered. The specification states at page 6 that the compounds of formula I exhibit valuable pharmacological properties such as agonism of S1P receptors as indicated by in vitro and in vivo tests. The specification then outlines various in vitro and in vivo tests and then state that compound of formula I deplete peripheral blood lymphocytes when administered at a dose of 0.03 to 3 mg/kg. There are no specific results for individual compounds. There

is no indication from the specification that the compound of the elected species exhibits results that are unexpected based on the teachings of Chiba.

Conclusion

Claims 1-2 and 6 are rejected. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kortney Klinkel whose telephone number is (571)270-5239. The examiner can normally be reached on Monday-Friday 8am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached at (571)272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

KLK

/Sharmila Gollamudi Landau/

Supervisory Patent Examiner, Art Unit 1611